

# Case of the Month

Angiomyolipoma Embolization in a Patient With TSC2/PKD1 Contiguous Gene Syndrome –  
A Case Report

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# Conflict of interest

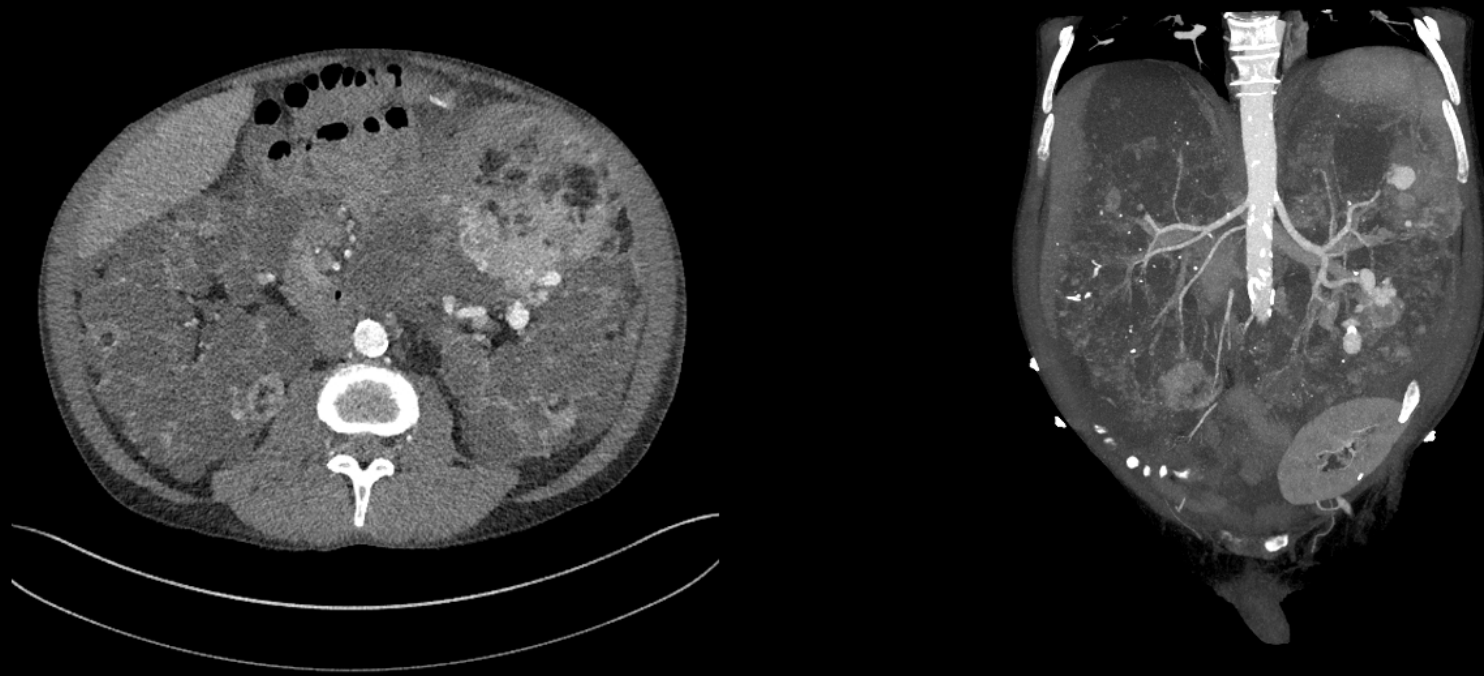
No conflict of interest to declare

# Case Presentation

A 58-year-old man was transferred from an outside hospital to our kidney transplantation unit with hypotension, fever, and low hemoglobin levels (66 g/L), compatible with **hypovolemic choc**

# Case Presentation

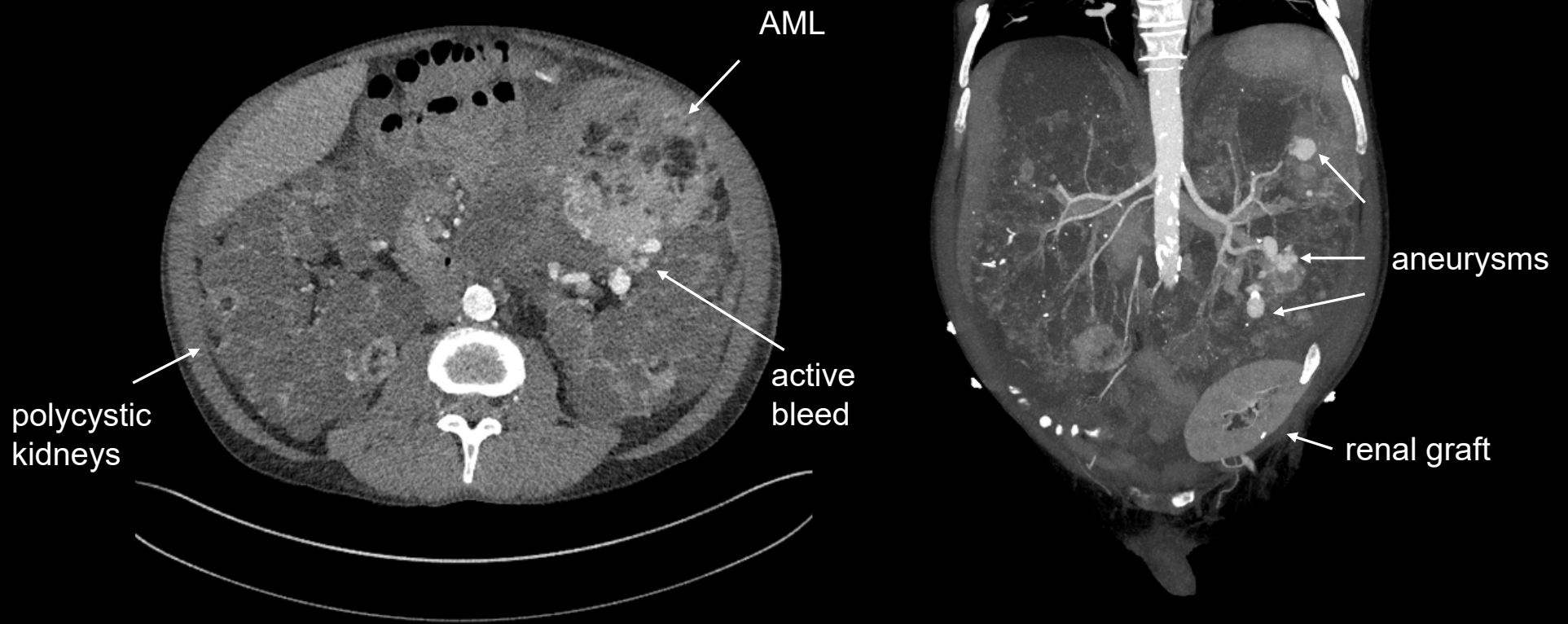
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# Case Presentation

Abdominal CT demonstrated multiple bilateral intraparenchymal renal aneurysms with **active contrast extravasation on the left kidney**. The aneurysms were arising within multiple fat-attenuation containing masses consistent with renal angiomyolipomas (AML). In addition, both kidneys were markedly enlarged, containing innumerable cysts of variable size.

# Case Presentation



# Case Presentation

The patient had received a cadaveric kidney graft for terminal renal failure due to **polycystic kidney disease (PKD)** 7 years ago. Antibody mediated renal allograft rejection and post transplant diabetes had complicated his post transplant clinical course. Baseline creatinine level was of 260  $\mu\text{mol/L}$  (GFR 24 mL/min)

A few years after the initial diagnosis of PKD, the patient developed multiple facial lesions and was referred to a dermatologist. The facial lesions were diagnosed as angiofibromas. It was then suspected the patient could also have **tuberous sclerosis complex (TSC)**

# Case Presentation

The impaired renal function poses a challenge in the context of multiple bleeding angiomyolipomas (AML), as iodine contrast digital subtraction angiography (DSA) can potentially worsen renal function, which was already borderline in this patient

Therefore, we decided to perform **proximal renal artery embolization** of the left kidney

# Case Presentation

Proximal renal artery embolization :

Advantage

- ✓ Significantly less iodine contrast used when compared to selective artery embolization of multiple branches

Disadvantage

- ✓ Complete infarction of kidney\*
- ✓ High risk of post embolization syndrome
- ✓ Increased risk of infection

*\*This was not an issue due to already non functioning left kidney*

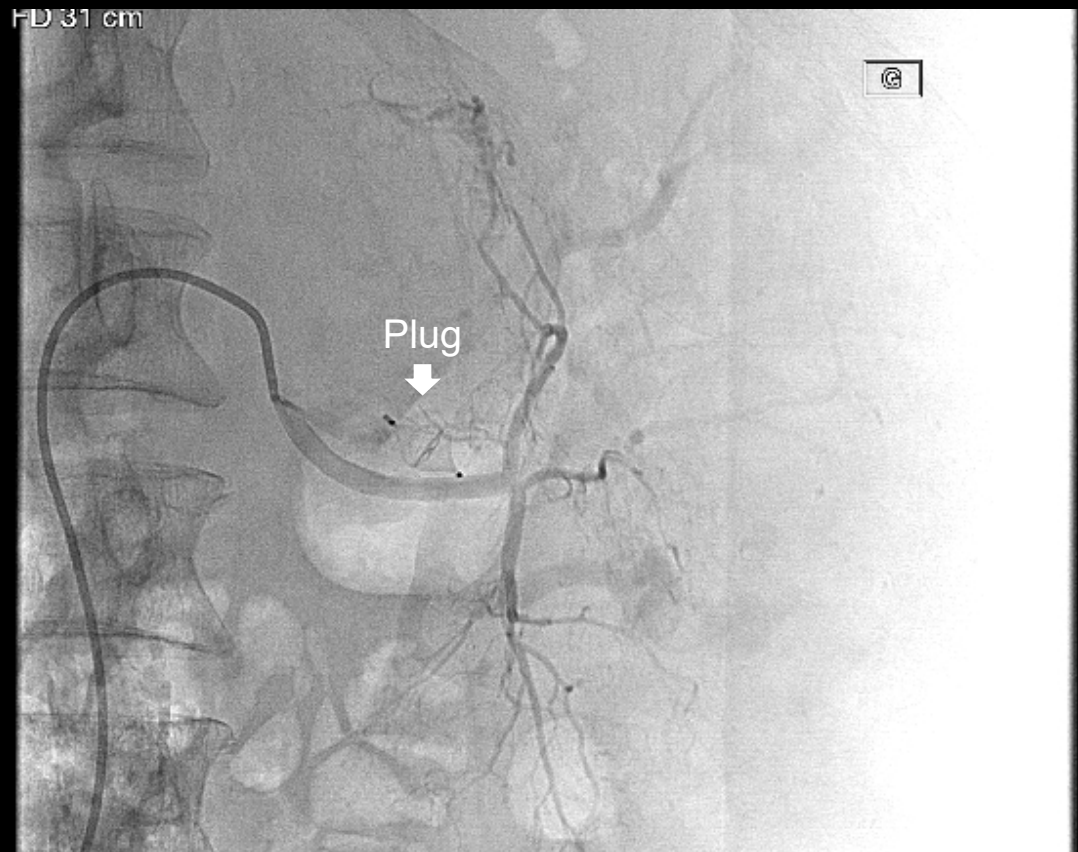
# Case Presentation

- Left common femoral artery access was obtained, and left renal artery was catheterized
- Diagnostic subtraction angiography showed multiple intra parenchymal renal aneurysms



# Case Presentation

- The anterior division of the renal artery was embolized with an 8 mm 4<sup>th</sup> generation Amplatzer Vascular Plug and multiple coils (Interlock Fibred IDC Occlusion System)



# Case Presentation

- The posterior division was then embolized with multiple coils (Interlock Fibrered IDC Occlusion System)



# Case Presentation

- Control angiogram showed complete embolization of the left renal artery



# Case Presentation

Day 1 after the procedure, the patient developed post-embolization syndrome and had severe pain, which required epidural anesthesia for pain control

Post-operative antibiotic coverage was provided for 5 days (Piperacillin-Tazobactam 3.375g IV q8h)

The patient recovered without additional complications and was discharged 5 days post procedure

# Case Presentation

At follow-up visit 8 months after the procedure, the patient was asymptomatic, and his hemoglobin and creatinine levels returned to baseline

A control CTA showed a decrease in size of the left kidney and of the angiomyolipomas



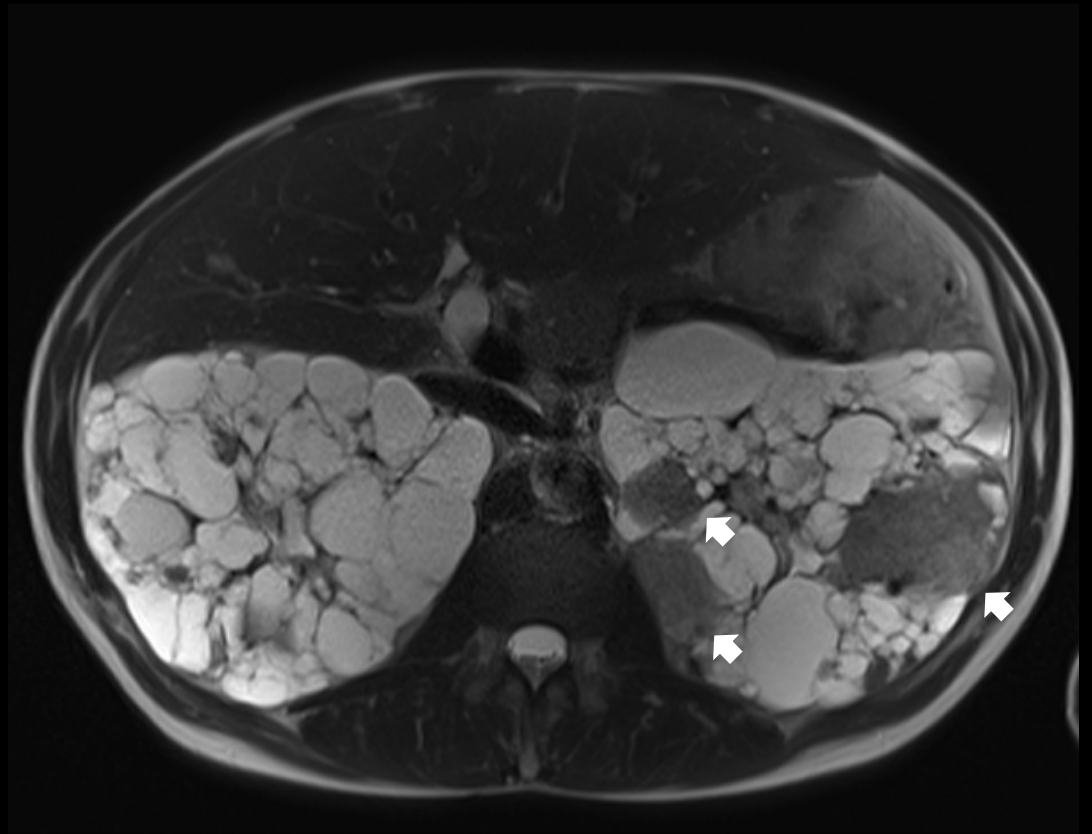
# Case Presentation

Retrospectively we asked ourselves :

- Why were the angiomyolipomas not detected on initial imaging? Would we have treated the patient at an earlier stage if we did?
- Why does the patient have two concomitant disease (PKD and TSC)?

# Case Presentation

The angiomyolipomas were present on the initial exam, but were interpreted as hemorrhagic cysts in a context of PKD (only T2 sequences were obtained on an MRCP)



# Angiomyolipomas

- Renal tumors comprised of perivascular epithelioid cells (PEComas)
- May occur sporadically or in association with TSC
- Prevalence in the general population estimated to be around 2.2%. Up to 80% in patients with TSC
  
- Most detected incidentally on imaging and asymptomatic
- Occasionally, complications such as hemorrhage, chronic kidney disease, hypertension or malignant transformation may occur
- In patients with TSC, the number and size of AMLs increases with age
  
- Imaging follow-up recommended due to potential of growth

# Angiomyolipomas

- In acute onset of life-threatening hemorrhage, selective renal artery embolization preferred over surgical intervention
- Bleeding AML in hemodynamically stable patients is also an indication for treatment
- Prophylactic treatment of large asymptomatic AMLs to prevent bleed has been described
  - AMLs larger than 4 cm (recent studies suggest that this value should possibly be larger to avoid unnecessary procedures)
  - Associated arterial aneurysm > 5mm.
- The favored treatment approach depends on the size and location of the AML, as well as the comorbidities of the patient. Available options include nephron-sparing surgery (NSS), selective renal artery embolization (SAE), radiofrequency ablation and cryoablation, and complete nephrectomy

# Angiomyolipomas

- In TSC patients with AMLs, medical treatment with everolimus, an mTOR inhibitor, is recommended as a first-line treatment for tumors larger than 3 cm in diameter. They have been effective to reduce tumor volume and risk of progression. Administration of everolimus should be used with caution in patients with reduced renal function, as renal tubular abnormalities have been observed in TSC patients treated with mTOR inhibitors

# Tuberous Sclerosis Complex

- Autosomal dominant genetic disorder
- Mutation in the *TSC1* gene (hamartin) or *TSC2* gene (tuberin)
- Rare disease, incidence of approximately 1:10 000 person
  
- Characterized by the development of benign hamartomas involving multiple organs, including the skin, brain, heart, kidney, lung and eyes :
  - ✓ hypomelanotic macules
  - ✓ facial angiofibromas
  - ✓ ungula fibromas
  - ✓ Shagreen patch
  - ✓ cortical tubers
  - ✓ subependymal nodules/subependymal giant cell astrocytoma (SGCT)
  - ✓ cardiac rhabdomyoma
  - ✓ angiomyolipomas
  - ✓ lymphangiomyomatosis

# Tuberous Sclerosis Complex

- Associated with a higher risk of malignancy, primarily in the kidneys, brain and soft tissues
- Most patients with TSC have epilepsy and neuropsychiatric disorders
- Management of the disease is focused on the surveillance and treatment of seizures, neuropsychiatric disorders, brain tumors and other systemic manifestations
- Everolimus, an mTOR inhibitor that has both immunosuppressive and antiproliferative effects, has been shown to be an effective treatment for various manifestations of TSC, including refractory epilepsy, symptomatic SGCT, renal angiomyolipomas, pulmonary lymphangiomyomatosis and facial angiofibromas

# Autosomal Dominant Polycystic Kidney Disease

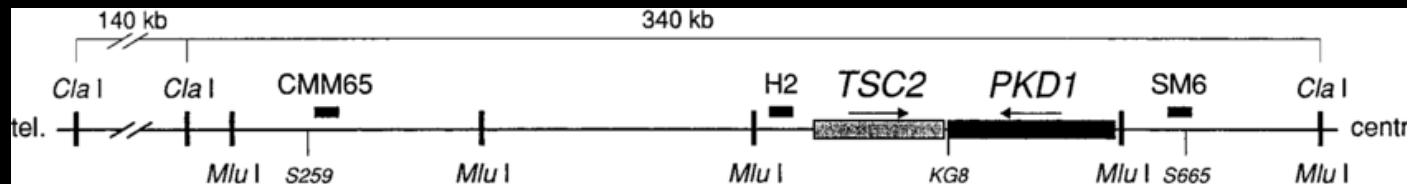
- Autosomal dominant genetic disorder
- Abnormality in the *PKD1* or *PKD2* gene
- Common disease, occurring in approximately 1:1000 individuals
- Accounts for about 5% of all cases of end stage renal failure
  
- The hallmark of ADPKD is the formation of cysts in ductal organs, particularly the kidney and liver
- Common renal complications include hypertension, hematuria, urinary tract infections, nephrolithiasis, chronic kidney pain and renal failure
- Major extrarenal manifestations comprise cerebral aneurysms, cardiac valvular disease, colonic diverticula and abdominal wall hernias
  
- The majority of patients will develop end stage renal failure and will eventually require kidney replacement therapy

# TSC2/PKD1 Contiguous Gene Syndrome

The *TSC2* gene lies immediately adjacent to *PKD1* gene in a tail-to-tail orientation on chromosome 16p13.3, separated by fewer than 100 base pairs. Deletions involving both genes result in a mixed phenotype involving features of both tuberous sclerosis and polycystic kidney disease. This association is known as TSC2/PKD1 contiguous gene syndrome, a well-known but rare disease, with very few cases reported in literature

Patients are usually diagnosed in early childhood, when stigmata of TSC, such as angiomyolipomas (AML), as well as findings of renal cystic disease are both present. Rarely, patients are diagnosed into adulthood, when manifestations such as hypertension and renal insufficiency appear

A more rapid progression to end-stage renal disease has been noted in patients with this disorder, with some cases requiring renal replacement therapy as early as the second decade of life



Longa et al.(1997). A large TSC2 and PKD1 gene deletion is associated with renal and extrarenal signs of autosomal dominant polycystic kidney disease. *Nephrology, dialysis, transplantation* : official publication of the European Dialysis and Transplant Association - European Renal Association. 12. 1900-7. 10.1093/ndt/12.9.1900.

# Case Discussion

We present a case of renal artery embolization to treat actively bleeding AMLs in a patient with a presumed TSC2/PKD1 contiguous gene syndrome

In hemodynamically unstable patients with bleeding AML, SAE is increasingly favored over NSS. Advantages include minimal invasiveness, feasibility of retreatment, decreased hospitalisation time and preservation of normal renal parenchyma

In this case, to minimize the amount of iodinated contrast used, in order to preserve renal graft function, embolization of the main branch of the left renal artery was chosen over sequential super-selective arterial embolization

Alternatively, usage of carbon dioxide (CO<sub>2</sub>) as an intravascular contrast agent would have made super-selective arterial embolization possible, as it is not nephrotoxic

# Conclusion

TSC2/PDK1 contiguous gene syndrome is a very rare disorder with manifestations associated with both tuberous sclerosis and polycystic kidney disease. It should be considered when patient present with characteristic findings of both syndromes. Management of complications of the disease is similar to patients with tuberous sclerosis or polycystic kidney disease

Selective artery embolization is often the first line of treatment for bleeding angiomyolipomas. Main renal artery embolization is associated with potential problems such as incomplete embolization, infection and post-embolization syndrome. Familiarity with these complications are crucial for optimal patient care

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